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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/628,322	07/28/2003	Beppino C. Giovanna	3603-030-03	4446
33432	7590	08/12/2005	EXAMINER	
KILYK & BOWERSOX, P.L.L.C. 53 A EAST LEE STREET WARRENTON, VA 20186			WEDDINGTON, KEVIN E	
			ART UNIT	PAPER NUMBER
			1614	

DATE MAILED: 08/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/628,322

Applicant(s)

GIOVANELLA ET AL.

Examiner

Kevin E. Weddington

Art Unit

1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 November 2004.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 4, 7 and 9-19 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 4, 7 and 9-19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

502

Art Unit: 1614

Claims 1, 4, ~~8~~⁷ and 9-19 are presented for examination.

Applicants' amendment and terminal disclaimers filed November 19, 2004 have been received and entered.

Accordingly, the rejections made under obviousness-type double patenting as set forth in the previous Office action dated August 23, 2004 at pages 2-9 are hereby withdrawn by the submissions of the terminal disclaimers.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4, 7 and 9-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating malignant melanoma with the oral administration of 20(S)-camptothecin or 9-nitro-20(S)-camptothecin at an effective dosage of 1 mg/kg/day, does not reasonably provide enablement for treating a malignant tumor in a mammal orally with a dose lower than 1.5 mg/kg/day or treating a malignant tumor with the other compounds such as 7-ethyl-1-carboxyloxy-camptothecin (camptothecin-11), 7-ethyl-10-hydroxy-20(S)-camptothecin, 9-chloro-20(S)-camptothecin, 9-bromo-20(S)-camptothecin, 9-hydroxy-20(S)-camptothecin, 11-hydroxy-20(S)-camptothecin, 10-hydroxy-20(S)-camptothecin, or mixture thereof.. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Art Unit: 1614

In this regard, the application disclosure and claims have been compared per factors indicated in the decision In re Wands, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation.

The factors include:

- 1) the quantity of experimentation necessary
- 2) the amount of direction or guidance provided
- 3) the presence or absence of working examples
- 4) the nature of the invention
- 5) the state of the art
- 6) the relative skill of those in the art
- 7) the predictability of the art and
- 8) the breadth of the claims

The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice that instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention, state of the prior art, relative skill of those in the art and the predictability of the art

The claimed invention relates to a method of treating a malignant tumor in a mammal comprising administering orally to said mammal in need of such treatment an effective amount of a water-insoluble camptothecin compound with a closed-lactone ring at a dose lower than 1.5 mg/kg/day, wherein said compound is selected from 20(S)-camptothecin, 9-nitro-20(S)-camptothecin, 7-ethyl-1-carbonyloxy-

Art Unit: 1614

camptothecin (camptothecin-11), 7-ethyl-10-hydroxy-20(S)-camptothecin, 9-chloro-20(S)-camptothecin, 9-bromo-20(S)-camptothecin, 9-hydroxy-20(S)-camptothecin, 11-hydroxy-20(S)-camptothecin, 10-hydroxy-20(S)-camptothecin, or mixture thereof.

The relative skill of those in the art is generally that of a Ph.D. or M.D.

The present invention is unpredictable unless experimentation is shown for the treatment of other malignant tumors with the said compounds of claim 1 by orally administering at the said dose lower than 1.5 mg/kg/day; and for the treatment of malignant tumors with orally administering 7-ethyl-1-carboxyloxy-camptothecin (camptothecin-11), 7-ethyl-10-hydroxy-20(S)-camptothecin, 9-chloro-20(S)-camptothecin, 9-bromo-20(S)-camptothecin, 9-hydroxy-20(S)-camptothecin, 11-hydroxy-20(S)-camptothecin, 10-hydroxy-20(S)-camptothecin, or mixture thereof.

The breadth of the claims

The claims are very broad and inclusive to all types of malignant tumors orally treated with the administration of compounds disclosed in claim 1.

The amount of direction or guidance provided and the presence or absence of working examples

The working examples set forth in Example 1, Table 1, show the administration of 20(S)-camptothecin and 9-nitro-20(S)-camptothecin, intramuscularly or intravenously at a dose of 4 mg/kg/day.

The working examples set forth in Example 1, Table 2, are limited to the oral administration of 20(S)-camptothecin, 9-amino-20(S)-camptothecin and 9-nitro-20(S)-camptothecin at a dose of 1 mg/kg/day to treated malignant melanoma only.

Art Unit: 1614

No examples showing the oral administration of the instant compounds disclosed in claim 1 to treat various malignant tumors set forth in claims 9-13 and 15-19 at a dose lower than 1.5 mg/kg/day.

The quantity of experimentation necessary

Applicants have failed to provide guidance as to how the treatment of other malignant tumors set forth in claims 9-13 and 15-19 with the said compounds of claim 1 by orally administering at the said dose lower than 1.5 mg/kg/day; and for the treatment of malignant tumors such as malignant melanoma with orally administering 7-ethyl-1-carboxyloxy-camptothecin (camptothecin-11), 7-ethyl-10-hydroxy-20(S)-camptothecin, 9-chloro-20(S)-camptothecin, 9-bromo-20(S)-camptothecin, 9-hydroxy-20(S)-camptothecin, 11-hydroxy-20(S)-camptothecin, 10-hydroxy-20(S)-camptothecin, or mixture thereof is undue. Therefore, undue experimentation would be required to practice the invention as it is claimed in its current scope.

Claims 1, 4, 7 and 9-19 are not allowed.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4, 7 and 9-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rendered indefinite by the phrase "a dose lower than 1.5 ma/kg/day" which can be interpreted that a dose of 0 mg/kg/day can be effective in the treatment of a malignant tumor.

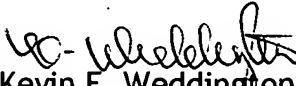
The remaining claims 4, 7 and 9-19 are rendered indefinite to the extent that they incorporate the above terminology.

Claims 1, 4, 7 and 9-19 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin E. Weddington whose telephone number is (571)272-0587. The examiner can normally be reached on 11:00 am-7:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571)272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Kevin E. Weddington
Primary Examiner
Art Unit 1614

Application/Control Number: 10/628,322

Page 7

Art Unit: 1614

K. Weddington

August 8, 2005